CLAIMS:

5

10

15

20

- 1. A device (1) for examination and use of an electrical field in a magnetic gradient field, containing magnetic particles in an examination area of an object under examination, comprising
- a. at least one first arrangement (2) for determining the spatial distribution of magnetic particles in at least one examination area of the object under examination, comprising a means (14) for generating a magnetic field with such a spatial magnetic field strength profile that a first sub-zone with low magnetic field strength and a second sub-zone with higher magnetic field strength are produced in at least one examination area, a means for detecting signals which depend on the magnetization in the object under examination, especially in the examination area, influenced by a local change in the particles, together with a means for evaluating the signals to obtain information about the, especially time-variable, spatial distribution of the magnetic particles in the examination area; and
- b. at least one second arrangement (8), comprising at least one electrical transmit and/or receive unit (6), comprising at least one voltage generator (22), at least one terminal contact (18) connected to the voltage generator and applicable and/or fastenable to an object under examination, and a ground terminal (20) applicable and/or fastenable to an object under examination.
- 2. A device (1) as claimed in claim 1, characterized in that the second arrangement (8) comprises at least one pair of contact electrodes (4), especially a plurality of pairs of contact electrodes, for recording potential differences.
 - 3. A device (1) as claimed in claim 1 or claim 2, characterized by at least one voltage measuring unit (24) and/or current measuring unit (26).

30

4. A device (1) as claimed in any one of the preceding claims, characterized in that the voltage generator (22), the voltage measuring unit (24) and/or the current measuring unit (26) may be brought into or are in active connection with a microprocessor or computer.

15

- 5. A device (1) as claimed in any one of the preceding claims, characterized in that the voltage measuring unit (24) and/or the current measuring unit (26) is/are equipped with at least one analog filter, measuring amplifier, A/D converter and/or digital filter.
- A device (1) as claimed in any one of the preceding claims, characterized in that a measuring voltage in the range of from 10 to 200 V may be generated with the voltage generator (22).
- 7. A device (1) as claimed in any one of the preceding claims, characterized by at least one frequency converter.
 - 8. A device (1) as claimed in any one of the preceding claims, characterized in that the means (14) for generating the magnetic field comprise a gradient coil arrangement for generating a magnetic gradient field which reverses direction in the first sub-zone of the examination area and exhibits a zero crossing.
 - 9. A device as claimed in any one of the preceding claims, characterized by a means for generating a time-variable magnetic field superimposed on the magnetic gradient field for the purpose of displacing the two sub-zones in the examination area.
 - 10. A device as claimed in any one of the preceding claims, characterized by a means, in particular at least one coil arrangement, for changing the spatial position of the two sub-zones in the examination area, such that the magnetization of the particles varies locally.
- 25 11. A device as claimed in any one of the preceding claims, characterized by a means, in particular a coil arrangement, for changing the spatial position of the two sub-zones in the examination area by means of superimposition of an oscillating or rotating magnetic field, especially in the first sub-zone with low field strength.
- A device as claimed in any one of the preceding claims, characterized by a coil arrangement for receiving signals induced by the variation over time of the magnetization in the examination area.
- 13. A device as claimed in any one of the preceding claims, characterized by at least one means for generating a first and at least one second magnetic field superimposed on

the magnetic gradient field, wherein the first magnetic field may be varied slowly over time

23

WO 2004/091390

10

15

20

25

30

35

PCT/IB2004/050448

with a high amplitude and the second magnetic field may be varied slowly over time with a low amplitude.

- A device as claimed in claim 13, characterized in that the two magnetic fields in the examination area may also extend substantially perpendicularly to one another.
 - 15. A method of determining the, especially three-dimensional, conductivity distribution, in an examination area of an object under examination using a device as claimed in any one of the preceding claims, comprising the introduction of magnetic particles into at least part of an examination area of the object under examination, generation of an electrical field at least in part of the examination area, generation of a magnetic field with such a spatial magnetic field strength profile that a first sub-zone with low magnetic field strength and a second sub-zone with higher magnetic field strength are produced in the examination area, variation of the spatial position of the two sub-zones in the examination area, such that the magnetization of the particles changes locally, the detection of signals which depend on the magnetization in the examination area influenced by this change, evaluation of the signals to obtain information about the, especially time-variable, spatial distribution of the magnetic particles in the examination area, and determination of the conductivity in the examination area as a function of the magnetization status of the magnetic particles.
 - 16. A method as claimed in claim 15, characterized in that the magnetic measuring voltage lies in the nanoVolt range, especially in the range above 5, preferably above 30 nV.

of an object under examination using a device as claimed in any one of claims 1 to 14, comprising the introduction of magnetic particles into at least part of an examination area of the object under examination, generation of an alternating electrical field at least in part of the examination area, generation of a magnetic field with such a spatial magnetic field strength profile that a first sub-zone with low magnetic field strength and a second sub-zone with higher magnetic field strength are produced in the examination area, variation of the spatial position of the two sub-zones in the examination area, such that the magnetization of the particles changes locally, in particular by means of superimposition of an oscillating or rotating magnetic field, wherein magnetic particles are used whose magnetic reversal is

WO 2004/091390 PCT/IB2004/050448

effected predominantly by means of geometric rotation or oscillation and which at least partially comprise an outer shell of an electrophoresis gel, which contains at least one active ingredient with at least one charged functional group, wherein the oscillation or rotational frequency of the magnetic field is matched to the frequency of the electrical field in such a way that the charge of the functional group of the active ingredient experiences a constant electrical field.

- A method as claimed in claim 17, characterized in that the frequency of the alternating electrical field lies in the range of from approximately 100 Hz to approximately 500 kHz and the oscillation or rotational frequency of the magnetic particles lies in the range of from approximately 100 Hz to approximately 1 MHz.
- A method of, especially locally targeted, electrostimulation in an examination area of an object under examination using a device as claimed in any one of claims 1 to 14, comprising the introduction of magnetic particles into at least part of an examination area of the object under examination, generation of an alternating electrical field at least in part of the examination area, generation of a magnetic field with such a spatial magnetic field strength profile that a first sub-zone with low magnetic field strength and a second sub-zone with higher magnetic field strength are produced in the examination area, variation of the spatial position of the two sub-zones in the examination area, such that the magnetization of the particles changes locally, especially by means of superimposition of an oscillating or rotating magnetic field, wherein magnetic particles are used whose magnetic reversal is effected predominantly by means of geometric rotation or oscillation and wherein the electrical field in the examination area is converted from a higher-frequency field into a lower-frequency field by interaction with rotating or oscillating particles.
- A method as claimed in claim 19, characterized in that the electrical field to be converted by oscillation or rotation exhibits a frequency in the range of from approximately 100 Hz to approximately 100 kHz.
- A method as claimed in claim 19 or claim 20, characterized in that the electrical field in the examination area is converted by interaction with the oscillating or rotating magnetic particles into a lower-frequency field with a frequency in the range of from approximately 1 Hz to approximately 500 Hz.

30

10

15

20

WO 2004/091390 PCT/IB2004/050448

- A method as claimed in any one of claims 15 to 21, characterized in that at least some of the magnetic particles exhibit anisotropic properties.
- 23. A method as claimed in any one of claims 15 to 22, characterized in that the effective anisotropy of the magnetic particles exhibits a value, which is sufficient for the magnetic reversal of the particle to take place substantially by geometric (Brownian) rotation.
 - A method as claimed in any one of claims 15 to 23, characterized in that the magnetic particle is a monodomain particle, which may be magnetically reversed substantially by means of Brownian rotation.

10

25

35

- A method as claimed in any one of claims 15 to 24, characterized in that the magnetic particle may be a hard- or soft-magnetic multidomain particle.
- A method as claimed in any one of claims 15 to 25, characterized in that the magnetic particles comprise hard-magnetic materials.
- A method as claimed in any one of claims 15 to 26, characterized in that the hard-magnetic materials constitute Al-Ni, Al-Ni-Co und Fe-Co-V alloys and/or barium ferrite (BaO 6xFe₂O₃).
 - A method as claimed in any one of claims 15 to 27, characterized in that the magnetic particles, in particular the ferromagnetic particles, are in the form of lamellae or needles.

Use of the device as claimed in any one of claims 1 to 14 for determining the, especially three-dimensional, conductivity distribution in the examination area of an object under examination.

- 30. Use of the device as claimed in any one of claims 1 to 14 for electrostimulation of neural pathways or muscles.
 - 31. Use of the device as claimed in any one of claims 1 to 14 for, especially locally targeted, drug and/or active ingredient release by means of electrophoresis.

- 32. Use as claimed in claim 31, characterized in that the drug comprises at least one charged functional group and is present in an electrophoresis gel layer, which surrounds the magnetic particle.
- Electro-physiologic contrast composition for magnetic particle imaging comprising electro-physiologic contrast particles that are capable of inducing anisotropic electric conductivity in the examination area and that comprise one or more magnetic particles.
- 10 34. Electro-physiologic contrast composition according to claim 33, wherein the electro-physiologic contrast particles have a main magnetic anisotropic direction and a main electric anisotropic direction which main magnetic anisotropic direction and main electric anisotropic direction are correlated such that, when the electric contrast particles align their main magnetic direction in an external magnetic field, also their electric anisotropy direction is at least partly aligned.
 - 35. Electro-physiologic contrast composition according to claim 34, wherein the main magnetic anisotropic direction is parallel with the main electric anisotropic direction.
- 20 36. Electro-physiologic contrast composition according to claims 33 to 35, wherein the electro-physiologic contrast particle has an anisotropic shape, preferably a disc like shape.
- Electro-physiologic contrast composition according to claim 33 to 36, wherein the electro-physiologic contrast particles comprise a disc shaped core of a material having a low conductivity that is covered with magnetic particles or a coating of a magnetic material.
 - Electro-physiologic contrast composition according to claim 36 are 37, wherein the ratio of the diameter to the thickness of the disc is between 0.005 and 0.8, preferably between 0.01 and 0.5.

30

39. Electro-physiologic contrast composition according to any one of claims 36 to 38, wherein the diameter of the disc is below 10 micrometers.

- 40. Electro-physiologic contrast composition according to claims 36 to 39, wherein the disc having a low conductivity is a red blood cell.
- Electro-physiologic contrast composition according to claims 33 to 35, wherein the electric contrast particles are needle shaped conductive multi-domain magnetic particles.
- 42. Electro-physiologic contrast composition according to any one of claims 33 to 41, wherein the magnetic particles are predominantly anisotropic magnetic particles having an average internal anisotropy field of at least 2mT
 - Electro-physiologic contrast composition according to claim 42, wherein the magnetic particles also comprise isotropic soft magnetic particles for concentration imaging contrast improvement.

15

- Method for imaging internal electric fields in a living organism, wherein at least 10 weight %, preferably 20 weight %, of the red blood cells in the blood of a patient are modified to form an electro-physiologic contrast composition according to claims 33 to 40.
- 20 45. Process for the manufacture of an electro-physiologic contrast composition according to claims 33 to 44, comprising aligning particles having electric anisotropic properties along a main electric anisotropic direction and depositing magnetic particles on said electric anisotropic particles in the presence of a magnetic field.
- 25 46. Process for the manufacture of electro-physiologic contrast composition according to claim 13, wherein the particles having electric anisotropic properties are disc shaped particles of a non conductive material, which disc shaped particles are aligned along a main electric anisotropic direction by depositing them substantially flat on a surface and wherein subsequently magnetic particles are deposited on the disc shaped particles in the presence of a magnetic field.
 - Method for imaging electrical resistivity or conductivity in an examination area comprising the steps of applying electrodes for generating and measuring electrical fields, introducing an electro-physiologic contrast composition according to anyone of claims 33 to 43 into the examination area, create an electrical field, scanning the examination area

point to spatially resolve the electrical conductivity or resistivity in the examination area.

28

PCT/IB2004/050448

WO 2004/091390

15

- Method for imaging internal electrical fields in an examination area comprising the steps of applying electrodes for measuring electrical fields, introducing an electro-physiologic composition according to anyone of claims 33 to 43, scanning the examination area with the field free region according to the method according to anyone of claims 15 to 28 and recording signals from the electric measurement electrodes as a function of the position of the field free point to spatially resolve the internal electrical fields in the examination area.
 - 49. Magnetic particle composition having a magnetization curve having a step change, the step change being characterized in that the magnetization change, as measured in an aqueous suspension, in a first field strength window of magnitude delta around the inflection point of said step change is at least a factor 3 higher than the magnetization change in the field strength windows of magnitude delta below or in the field strength windows of magnitude delta above the first field strength window, wherein delta is less than 2000 microtesla and wherein the time in which the magnetisation step change is completed in the first delta window is less than 0.01 seconds.
 - 50. Use of the magnetic particle composition according to claim 49 in a method according to anyone of claims 15 to 28 or 47 to 48.
- Electro-physiologic contrast composition according to anyone of claims 33 to 43, wherein the magnetic particles are a magnetic particle composition according to claim 49.